Pharmacological prevention of venous thromboembolism in orthopaedic surgery

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Summary

The prophylaxis of venous thromboembolism (VTE) with anticoagulant drugs is a long-established practice in hip and knee replacement surgery, as well as in the treatment of femoral neck fractures, while there are few data regarding the prevention of VTE in other fields of orthopaedic surgery and traumatology. In order to provide practical recommendations for daily management of VTE prophylaxis in orthopaedic patients, recently the Italian Societies of Thrombosis and Haemostasis, Orthopaedics and Traumatology and Anaesthesia have drawn up a first Intersociety Consensus on antithrombotic prophylaxis in total hip and knee replacement surgery, and in the treatment of femoral neck fracture, then updated in 2013, and a subsequent Intersocietary Consensus, in cooperation also with the Society of general practitioners, concerning antithrombotic prophylaxis in other types of orthopaedic surgery and traumatology. Before starting any prophylactic treatment it is of crucial importance the assessment of both thrombotic and bleeding risk of patients undergoing surgery. Thromboembolic prophylaxis is recommended with low molecular weight heparins (LMWH), fondaparinux (FON) or with the new oral anticoagulants (NOA) in patients undergoing hip and knee replacement surgery while patients undergoing treatment of femoral neck fracture should be treated with LMWH or FON. Regarding the non-prosthetic orthopaedic surgery and traumatology, it is recommended prophylaxis with LMWH or FON in situations of high thromboembolic risk or in the case of interventions or trauma involving pelvis, acetabulum or knee.

KEY WORDS: prevention of venous thromboembolism; total hip replacement; total knee replacement; femoral neck fractures; anticoagulant prophylaxis.

Introduction

Venous thromboembolism (VTE) has a significant clinical and social impact due to its high incidence and possibly severe sequelae. Pulmonary embolism (PE), with or without concomitant detectable deep vein thrombosis (DVT), is the direct cause of roughly 10% of hospital deaths (1). Although anticoagulant prophylaxis for VTE has been routine practice for a long time, the literature on this topic is by no means comprehensive and unequivocal, especially in orthopaedic and trauma surgery. In fact, although the existing guidelines (ACCP (1) and NICE (2)) have been recently revised and updated by authoritative working groups using rigorous scientific method, they are complex documents that are not particularly clinician-friendly. Furthermore, the chapters on musculoskeletal pathologies and orthopaedic surgery cover only a small number of the wide range of pathologies and treatments that clinicians have to manage on a daily basis. This prompted SIISET (the Italian Society for the Study of Thrombosis and Haemostasis), SIO (the Italian Society of Orthopaedics and Traumatology), OTODI (the Italian Association of Hospital Orthopaedics and Traumatology) and SIAARTI (the Italian Society of Anaesthesia, Analgesia, Resuscitation and Intensive Care) to set up a working group in 2009 to define an inter-association consensus statement (3) providing practical recommendations for the daily management of VTE prophylaxis in hip (HR) and knee (KR) replacement surgeries and in patients with femoral neck fractures (FNF). The publication and success of this consensus document, updated in 2013 (4), led to write up a similar document (5), this time in cooperation also with SIMG (the Italian Society of General Medicine) regarding VTE prophylaxis in the remaining major orthopaedic surgeries, the so-called minor orthopaedic surgery and orthopaedic trauma, in order to provide a comprehensive series of practical and easily applicable advices to further widespread good clinical practice in the field.

Risk stratification of patients

Before starting any prophylactic treatment, it is crucial to assess, on one hand, the thrombotic risk and, on the other, the bleeding risk of patients undergoing orthopaedic surgery in order to identify those patients at high VTE risk in which the pharmacological approach is contraindicated or should be practiced with caution. The risk of VTE is conditioned by the interaction of two types of factors: (a) individual risk factors, linked to the conditions and characteristics of the patients themselves (e.g. individual or family history of VTE, known congenital or acquired thrombophilia, active cancer or cancer treatment, prolonged immobilization, age, pregnancy, puerperium, oestrogen contraceptive or hormone replacement therapy); (b) treatment-related factors, arising from the specific features and consequences of the surgical or non-
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VTE prophylaxis in hip and knee replacement and in femoral neck fracture surgery

Concerning HR and KR, pharmacological prophylaxis is based on low-molecular-weight heparin (LMWH), fondaparinux (FON), and new oral anticoagulants (NOA). According to this Italian Consensus, unfractionated heparin (UH) must not be used for VTE prophylaxis considering that its efficacy is lower than that of LMWH, it has a short half-life, and it more frequently induces thrombocytopenia and, despite recommendations of last edition of ACCP guidelines (1), aspirin must not be used too.

Table 1 - High haemorrhagic risk factors (decisions on an individual case basis) (1, 3, 16, 17) (modified from Randelli F, et al. 2013).

- Individual or family history of major haemorrhage
- Acquired coagulopathies (e.g., hepatic insufficiency with abnormal coagulation test results and/or platelet count)
- PT ratio or PT-INR >1.5
- APTT >1.25 (except in cases with antiphospholipid antibodies and no history of haemorrhage)
- Thrombocytopenia (<50,000/microL)
- Severe renal failure (creatinine clearance <30 mL/min)
- Cerebral metastases or cerebral angioma at risk of bleeding (confirmed by CT angiography or MRI)
- Recent haemorrhagic stroke or ischemic stroke (24 h)
- Gastric and/or genitourinary or ocular haemorrhage within the previous 2 weeks
- Medicines acting on haemostasis (e.g., anti-platelet, anti-inflammatory drugs)
- Ill degree arterial hypertension (230/120 mmHg)
- Acute infectious endocarditis (except that due to mechanical prostheses)

surgical procedure employed (e.g. the position of the patient on the operating table, particularly if prone, any forced twisting or traction of a limb that could damage the blood vessels, the use of additional medical devices, the length of time before the patient returns to normal ambulation) (5). Unlike the more precise and individual stratification of thrombotic risk, the definition of bleeding risk is often limited to mere suggestions, ‘empirical’ recommendations, frequently not supported by clinical trials. Contraindications to pharmacological VTE prophylaxis are reported as absolute or relative, but even in the definition of the absolute recommendations there is some discrepancy between different sources. Anyway, we defined as absolute contraindications to pharmacological prophylaxis active bleeding and untreated congenital coagulopathies (haemophilia and severe von Willebrand disease) (1, 2, 6, 7); in these patients it is advisable to use mechanical devices such as graduated compression stockings (GCS) or, in cases of high thrombotic risk, intermittent pneumatic compression (IPC) or plantar venous pump (PVP). Instead, in case of acquired coagulopathies and other conditions at increased risk of bleeding (1, 2, 6, 7) (Table 1), physicians must accurately assess the risk/benefit ratio and start pharmacological antithrombotic prophylaxis as soon as the haemorrhagic risk is under control, for as long as the thrombotic risk persists. Particular attention should also be given to fragile patients (body weight <50 kg, age>75 years, moderate chronic renal failure i.e. creatinine clearance 30–50 ml/min), who require individualized treatment (5).

VTE prophylaxis in the remaining types of major orthopaedic surgery (other than HR, KR and FNF), minor orthopaedic surgeries and traumatology

In minor orthopaedic surgery and trauma cases, pharmacological VTE prophylaxis is indicated in situations of high thromboembolic risk or in the case of interventions or trauma involving pelvis, acetabulum or knee and is essentially based on LMWH (bemiparin, dalteparin, enoxaparin, nadroparin, parnaparin or reviparin), although UH can be used in certain cases (3). As regards LMWH administration, although scientific studies identifying the optimal dose have not yet been published, it is advisable to give high prophylactic doses (>3400 IU/day).
Lower doses should, however, be considered in “fragile” patients (e.g., low body weight, renal insufficiency). Concerning the timing of prophylaxis, there is evidence in the literature about the differences in terms of efficacy and safety of pre-surgical and post-surgical LMWH administration in arthroscopic surgery, while in non-arthroscopic orthopaedic surgery the post-operative start of prophylaxis is advisable. For trauma emergency surgery the same recommendations as for FNF should be followed (3), while in non-surgical traumatology, antithrombotic prophylaxis, when indicated, should be started upon non-weight bearing and/or application of the cast or splint, etc. (5). In elective spinal surgery, pharmacological prophylaxis (LMWH) should be considered only in cases of prolonged and/or complex surgery (e.g., combined anterior and posterior approaches) and in patients with relevant VTE risk factors. In all these cases, pharmacological prophylaxis should be administered for a minimum of 7 days. The duration of the prophylaxis should also take into account the persistence of thromboembolic risk factors and the recovery of mobility and weight bearing (at least 10-20 kg) (5). An important novelty on the horizon is represented by NOAs which have been recently trialed. Although there are no scheduled trials of these drugs in VTE prevention in situations not involving hip and knee replacement surgery, the expected increased diffusion of new drugs for stroke prevention in atrial fibrillation will doubtlessly increase the number of patients on NOAs needing orthopaedic surgery (5).

References

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